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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 09/712,638   | 11/14/2000  | Isidore Rigoutsos    | YOR920000435US1     | 8850             |
| 48062  | 7590        | 12/12/2006           | EXAMINER            |                  |
| RYAN, MASON & LEWIS, LLP<br>1300 POST ROAD<br>SUITE 205<br>FAIRFIELD, CT 06824 |             |                      | LY, CHEYNE D        |                  |
|  |             |                      | ART UNIT            | PAPER NUMBER     |
|  |             |                      | 2168                |                  |

DATE MAILED: 12/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

|  |   |  |  |
|--|---|--|--|
| <p align="center"><b>Office Action Summary</b></p> | <p><b>Application No.</b></p> <p>09/712,638</p> | <p><b>Applicant(s)</b></p> <p>RIGOUTSOS ET AL.</p> |  |
|  | <p><b>Examiner</b></p> <p>Cheyne D. Ly</p>      | <p><b>Art Unit</b></p> <p>2168</p>                 |  |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 November 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-6, 8-12, 23 and 25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6, 8-12, 23, and 25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 21, 2006 has been entered.
2. The rejection of record are hereby withdrawn as necessitated by the Decision on Appeal, mailed September 22, 2006, and the amendment, filed November 21, 2006. The instant rejections are newly applied.
3. Applicant's arguments are moot in view of the amended claims which necessitated the withdrawal of the rejections of record.
4. Claims 1-6, 8-12, 23, and 25 are examined on the merits.

### **CLAIM REJECTIONS - 35 USC § 103**

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.
6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were

made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-6, 8, 10, 11, 23, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rigoutsos et al. (1998) taken with IUPAC-IUB Joint Commission of Biochemical Nomenclature (JCBN) (1983).

#### **MOTIVATION TO COMBINE**

8. Rigoutsos describes a new algorithm for the discovery of rigid patterns (motifs) in biological sequences (page 55, Abstract etc.) wherein the sequences are defined by the alphabet of residues represented by one-letter codes (e.g. the set of all amino acids). It is well known in the art that the set of all amino acids comprises B for aspartic acid or asparagine (at least two symbols), X for unknown or other amino acid, or Z for glutamic acid or glutamine (JCBN, pages 5-6). Therefore, one of ordinary skill in the art at the time of the invention would have been motivated by Rigoutsos to include in the alphabet of residues B for aspartic acid or asparagine (at least two symbols), X for unknown or other amino acid, or Z for glutamic acid or glutamine as described by JCBN.

#### **PRIOR ART**

9. In regard to claim 1, Rigoutsos describes a method comprising the steps of:

Providing a set of sequences (page 59, column 1, last paragraph), wherein the sequences are not aligned (page 59, column 1, last paragraph, especially, core histones (H3 and H4); and each sequence comprises a series of symbols (page 60, column 2, Table 2);

Discovering a plurality of patterns common to a plurality of the sequences, wherein each pattern comprises a plurality of positions, at least one of the positions comprise an expected symbol (page 56, column 1, Methods section, to page 59, column 1, next to the last paragraph);

Determining if a candidate sequence comprises a predetermined number of the patterns (page 60, column 1, last paragraph, to column 2, last line).

10. However, Rigoutsos does not describe the limitation of “and at least one of the positions comprise one symbol of a specified plurality of symbols, wherein the specified plurality of symbols consist of at least two symbols and no more than...available symbols in a set.” It is well known in the art that the set of all amino acids comprises B for aspartic acid or asparagine (at least two symbols), X for unknown or other amino acid, or Z for glutamic acid or glutamine (JCBN, pages 5-6). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to apply the new algorithm by Rigoutsos to include in the alphabet of residues B for aspartic acid or asparagine (at least two symbols), X for unknown or other amino acid, or Z for glutamic acid or glutamine as described by JCBN.
11. In regard to claim 2, Rigoutsos describes the patterns common to a plurality of the set of sequences comprise test patterns (page 59, column 2, especially, “the existence of the core histone motif...”), wherein the sequences in set of sequences comprise test

sequences (page 59, column 2, last paragraph, especially, “selected representative subsets from both families”), and wherein the step of determining if a candidate sequence comprises a predetermined number of the patterns comprises the step of determining if there are candidate patterns in the candidate sequence that match all of the predetermined number of test patterns (page 60, columns 1-2, especially, “searched SwissProt...for sequences matching the most descriptive among these patterns...”).

12. In regard to claims 3 and 8, Rigoutsos describes the step of determining if each of the plurality of patterns is statistically significant (page 62, column 1, last paragraph, to column 2, last paragraph, especially, “only proteins with a probability of  $<0.005$  were retained for further processing”).
13. In regard to claim 4, Rigoutsos describes discovering is performed without using any knowledge about biological information related to family, cardinality or image characteristics of sequences in the set of unaligned sequences (page 65, column 2, especially, “the absence of any context information”, and page 66, column 1, lines 10-22, especially “sequences that do not necessarily all belong to a single group”).
14. In regard to claim 6, Rigoutsos describes some of the plurality of positions comprise positions which may be occupied by any sequence character (page 56, column 2, lines 1-10, especially, “don’t care character”).
15. In regard to claim 10, Rigoutsos discloses if each of the plurality of patterns is statistically significant further comprises the steps of removing instances of each of the patterns from the set of sequences to create a new set of sequences and performing the

step of discovering on the new set of sequences (page 59, column 1, lines 1-42, especially, "then R is discarded...").

16. In regard to claim 11, Rigoutsos describes the steps of if any of the patterns is statistically significant, selecting a statistically significant pattern, modifying a composite descriptor to include the selected pattern if the selected pattern is not already part of the composite descriptor, and continuing to select statistically significant patterns until all statistically significant patterns have been selected (page 57, columns 1-2, The algorithm section, especially, "combine together...patterns", to page 59, line 42, "produces all the maximal...patterns satisfying the minimum support requirement."
17. In regard to claims 23 and 25, Rigoutsos in view of JCBN renders said claims obvious over the above cited because the TEIRESIAS algorithm is implemented on an IBM Power-PC workstation (page 60, column 1, line 5-7).
18. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rigoutsos et al. (1998) taken with IUPAC-IUB Joint Commission of Biochemical Nomenclature (JCBN) (1983) as applied to claims 1-6, 8, 10, 11, 23, and 25, in further view of Stormo (January 2000).
19. In regard to claim 5, Rigoutsos describes the motivation of the Teiresias algorithm is to address the importance of the discovery of motifs in biological sequences (page 55, Abstract etc.). It is well known in the art that the set of all amino acids comprises B for aspartic acid or asparagine (at least two symbols), X for unknown or other amino acid, or Z for glutamic acid or glutamine (JCBN, pages 5-6). While, Stormo describes the Teiresias algorithm is one of a variety of algorithms designed to identify consensus

sequences from unaligned DNA sequence...The alternative approach is to search directly for a weight matrix...using a greedy algorithm that builds up an entire alignment of the sites by adding in new ones at each iteration (page 20, column 1, line 7, to column 2, line 10). One of ordinary skill in the art at the time of the invention would have been motivated by Rigoutsos to use the Teiresias algorithm to address importance of the discovery of motifs in biological sequences with the adding in new ones at each iteration. Therefore, it would have been obvious to one of ordinary skill in the art to make and use the method and system described by Rigoutsos with the adding in new ones at each iteration described by Stormo.

20. Claims 9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rigoutsos et al. (1998) taken with IUPAC-IUB Joint Commission of Biochemical Nomenclature (JCBN) (1983) as applied to claims 1-6, 8, 10, 11, 23, and 25, in further view of Wu et al. (March 2000).

#### **MOTIVATION TO COMBINE**

21. Wu describes a pattern-based approach for increasing the speed of sequence analysis using scoring matrices (Abstract etc. and page 243, column 1, lines 3-27). It is well known in the art that the set of all amino acids comprises B for aspartic acid or asparagine (at least two symbols), X for unknown or other amino acid, or Z for glutamic acid or glutamine (JCBN, pages 5-6). While, Rigoutsos describes the Teiresias algorithm to address the importance of the discovery of motifs in biological sequences (page 55, Abstract etc.). Therefore, one of ordinary skill in the art at the time of the invention



would have been motivate Wu to improve the algorithm of Rigoutsos to increase the speed of sequence analysis.

#### **PRIOR ART**

22. In regard to claim 9, Rigoutsos and JCBN describe all the limitation of said claim except for the limitation of “using a second-order Markov chain method...” Wu describes the use of the second-order Markov chain method to increase the speed of sequence analysis base do patterns (page 233, column 1, last 3 lines, to column 2, line 7, and page 240, column 1, lines 1-4). Therefore, it would have been obvious to use the described by Rigoutsos and JCBN with the second-order Markov chain method of Wu to increase the speed of sequence analysis.

23. In regard to claim 12, Rigoutsos and JCBN describe all the limitation of said claim except for the further limiting steps of claim 12. Wu describes the method of specifying a probability threshold (page 233, column 2, last paragraph, to page 234, column 1, lines 1-19, and page 236, column 1, Significance filtering section, to page 237, column 1, line 20). Therefore, it would have been obvious to use the method described by Rigoutsos and JCBN in further view of Wu to increase the speed of sequence analysis.


#### **CONCLUSION**

24. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your

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application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

25. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The USPTO's official fax number is 571-272-8300.
26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.
27. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tim Vo, can be reached on (571) 272-3642.

C. Dune Ly   
Patent Examiner  
12/9/06